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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
08/599,974	02/14/1996	JEFFREY M. FRIEDMAN	600-1-162CP1	1513

7590 01/15/2004

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EXAMINER	
O HARA, EILEEN B	

ART UNIT	PAPER NUMBER
1646	

DATE MAILED: 01/15/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	08/599,974	FRIEDMAN ET AL.	
	Examiner	Art Unit	
	Eileen O'Hara	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 October 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-19,21,22 and 24-68* is/are pending in the application.

4a) Of the above claim(s) *1-19,25,29-33,49,50,53-66 and 68* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *21, 22, 24, 26-28, 34-48, 51, 52 and 67* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-19,21,22 and 24-68* are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *11/27/00* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. Claims 1-19, 21, 22 and 24-68 are pending in the instant application.

Election/Restrictions

2. Applicant's election with traverse of Group V, drawn to nucleic acids encoding murine splice variant OB-Re polypeptides, vectors, host cells and method of producing polypeptide, in the Paper filed Nov. 25, is acknowledged. The traversal is on the ground(s) that even with patentably distinct inventions, restriction is not required unless one of the following reasons appear (MPEP 808.2): 1) separate classification, 2) separate status in the art; or 3) different field of search. Applicants additionally point out that under Patent Office examining procedures, "If the search and examination of an entire application can be made without serious burden, the Examiner is encouraged to examine it on the merits, even though it includes claims to distinct or independent inventions" (MPEP 803< Rev. 8, May 1988). Applicants submit that the claims of Group V are fundamentally related to nucleic acids encoding murine splice variants OB-Ra, OB-Rb, OB-Rc and OB-Rd, respectively of Groups I-IV, and that the search for any of the nucleic acids separately classified by the Examiner as the invention of Group V would require an additional search of the identical classes, thus resulting in a duplicate search for the same material, and therefore Applicants submit that the Search and Examination of the entire Application, or at least, of Groups I-V, can be made without serious burden.

This is not found persuasive because under MPEP § 803, there are two criteria for a proper requirement for restriction between patentably distinct inventions:

(A) The inventions must be independent (see MPEP § 8702.01, 806.04, 808.01) **or** distinct as claimed (see MPEP § 806.05 - § 806.05(I): and

(B) There must be a serious burden on the examiner if restriction is required (see MPEP § 803.02, § 806.04(a) - § 806.04(I), § 808.01(a), and § 808.02).

Consistent with current patent practice, a serious search burden may be established by (A) separate classification thereof: (B) a separate status in the art when they are classifiable together: (C) a different field of search:. Even though there is significant overlap between the sequences, the splice variants of the different groups would require separate sequence searches, which would be a different field of search for each group. Thus, the groups require divergent searches, and to search all inventions would be burdensome.

Applicant's election of nucleic acids encoding a hybrid OB-Re receptor wherein the N-terminal sequence is amino acid residues 28-796 (SEQ ID NO: 87) and the C-terminal sequence is NO: 15 after His 796 (SEQ ID NO: 91), wherein the numbering is based on the amino acid sequence of SEQ ID NO: 55 in the Paper filed Oct. 27, 2003 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

The requirement is still deemed proper and is therefore made FINAL.

Claims 1-19, 25, 29-33, 49, 50, 53-66 and 68 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 20.

Claims 21, 22, 24, 26-28, 34-48, 51, 52 and 67 are currently under examination and will be examined as far as they relate to the OB-Re splice variant of SEQ ID NO: 10.

Advisory Information

3. Claims 21, 22, 24, 26-28, 34-48, 51, 52 and 67 are being examined as they are drawn only to nucleic acid molecules of SEQ ID NO: 9 or a nucleic acid which codes on expression for a polypeptide of SEQ ID NO: 10. (claim 27, section a and section c. viii, 8, ix (5)).

Specification

4.1 The disclosure is objected to because of the following informalities: on page 25, line 11, "JAC" should be "JAK".

Appropriate correction is required.

4.2 The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed.

The following title is suggested: Nucleic Acids Encoding DB, The Receptor For LEPTIN.

Claim Objections

5.1 Claims 21, 24, 27, 28 and 67 are objected to because of the following informalities: they encompass non-elected inventions, which should be deleted. Appropriate correction is required.

5.2 Claims 27 is objected to because it is not in sequence compliance. The elected invention of claim 27 encompasses nucleic acids encoding a (hybrid) leptin (OB-Re) polypeptide wherein the N-terminal sequence is amino acid residues 28-796 (SEQ ID NO: 87) and the C-terminal

sequence is NO: 15 after His 796 (SEQ ID NO: 91), wherein the numbering is based on the amino acid sequence of SEQ ID NO: 55. Claim 27 does not comply with 37 CFR j 1.822(e) which states that (a) sequence that is made up of one or more noncontiguous segments of a larger sequence or segments from different sequences shall be presented as a separate sequence". However, the elected hybrid leptin polypeptide is identical to the polypeptide of SEQ ID NO: 10, with the exception that it is lacking the first 27 amino acids of SEQ ID NO: 10. For clarity, it is recommended that the claim be amended to claim the nucleic acids encoding the hybrid as follows: "leptin receptor polypeptide consisting of amino acids 28-805 of SEQ ID NO: 10". Otherwise, a new CRF and sequence listing will be required that recite the elected hybrid by a separate SEQ ID NO:, and the claims and the instant specification would also need to be amended so that they comply with 37 C.F.R. j 1.821(d) which requires a reference to that particular sequence identifier (SEQ ID NO:) be made in the specification and claims wherever a reference is made to that sequence. For rules interpretation Applicant may call (703) 308-1123. See M.P.E.P. 2422.04.

If applicants elect to claim the hybrid receptor this way, the specification would also need to be amended so that it identifies the hybrid in the same way. This would not constitute new matter.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

6. Claims 21, 22, 24, 26-28, 34-48, 51, 52 and 67 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 29-31 of copending Application No. 08/783,734. Although the conflicting claims are not identical, they are not patentably distinct from each other because they are both drawn to nucleic acid molecules of SEQ ID NO: 9 or encoding the protein of SEQ ID NO: 10, and it would be *prima facie* obvious to one of ordinary skill in the art to express those nucleic acids in vectors and host cells, and to recombinantly produce the encoded protein.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

7. Claim 28 is rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. Claim 28, as written, does not sufficiently distinguish over nucleic acid molecules encoding leptin receptors as they exist naturally because the claim does not particularly point out any non-naturally occurring differences between the claimed products and

the naturally occurring products. In the absence of the hand of man, the naturally occurring products are considered non-statutory subject matter. See *Diamond v. Chakrabarty*, 447 U.S. 303, 206 USPQ 193 (1980). The claims should be amended to indicate the hand of the inventor, e.g., by insertion of "isolated". See MPEP 2105.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claims 21, 22, 24, 26-27, 34-48, 51, 52 and 67 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The specification describes a polypeptide sequence consisting of SEQ ID NO: 55, which is the murine full-length leptin (OB) receptor, and a splice variant (SEQ ID NO: 10) that is a soluble form of the full-length receptor. The claims are directed to nucleic acids encoding the splice variant of SEQ ID NO: 10, which is shown to have the following activity: binding leptin. However, the claims as written include nucleic acids encoding polypeptides comprising fragments and homologues, encompass nucleic acids encoding polypeptides that vary substantially in length and also in amino acid composition. The instant disclosure of a nucleic acid encoding the full-length protein, that of SEQ ID NO: 55, and nucleic acids encoding the splice variants, all of which are identical to at least amino acids 1-664 of SEQ ID NO: 55, which is the majority of the extracellular domain, does not adequately

support the scope of the claimed genus, which encompasses a substantial variety of subgenera. A genus claim may be supported by a representative number of species as set forth in *Regents of the University of California v Eli Lilly & Co,* 119F3d 1559, 1569, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997), which states:

"To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention". Lockwood v. American Airlines, Inc., 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (1997); In re Gosteli, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1980) ("[T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed.") Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." Lockwood, 107 F.3d 1565, 1572, 41 USPQ2d at 1966.

An adequate written description of a DNA, such as the cDNA of the recombinant plasmids and microorganisms of the '525 patent, "requires a precise definition, such as by structure, formula, chemical name, or physical properties," not a mere wish or plan for obtaining the claimed chemical invention. Fiers v. Revel, 984 F.2d 1164, 1171, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993). Accordingly, "an adequate written description of a DNA requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it; what is required is a description of the DNA itself." Id at 1170, 25 USPQ2d at 1606."

A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus, or of a recitation of structural features common to the genus, which features constitute a substantial portion of the genus. The instant specification discloses, however, an isolated polypeptide sequence SEQ ID NO: 55 and five splice variants. Receptor function, however,

cannot be reliably predicted from protein sequence homology. For example, Transforming Growth Factor (TGF-beta) Family OP-1 induces metanephrongenesis whereas closely related TGF-beta family members-BMP-2 and TGF-beta1-have no effect on metanephrogenesis under identical conditions (Vukicevic et al., 1996, PNAS USA 93:9021-9026). Platelet-derived Growth Factor (PDGF) Family VEGF, a member of the PDGF family, is mitogenic for vascular endothelial cells but not for vascular smooth muscle cells while PDGF is mitogenic for vascular smooth muscle cells but not for vascular endothelial cells (Tischer et al., U.S. Patent 5,194,596, column 2, line 46 to column 3, line 2). Finally, vertebrate growth hormone of 198 amino acids becomes an antagonist (inhibitor of growth) when a single amino acid is changed (Kopchick et al, U.S. Patent No. 5,350,836). Even 99% homology does not allow predictability in this instance. Given the unpredictability of homology comparisons, and the fact that the specification fails to provide objective evidence that the additional sequences are indeed species of the claimed genus it cannot be established that a representative number of species have been disclosed to support the genus claim. No activity is set forth for the additional sequences. The instantly claimed genus is not so limited and the prior art does not provide compensatory structural or correlative teachings to enable one of skill to identify the nucleic acids encompassed.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

9.1 Claims 24, 36, 38, 40, 42, 44, 46, 48 and 52 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 24, 36, 38, 40, 42, 44, 46, 48 and 52 are indefinite because independent claim 24 encompasses a nucleic acid molecule which "hybridizes" to the DNA molecule of SEQ ID NO: 9 or the complement thereof. Though the specification on pages 39-40 describes various hybridization and wash conditions, they are exemplary. The term "hybridizes" is considered indefinite, since the resulting claim does not clearly set forth the metes and bounds of the patent protection desired.

9.2 Claims 21, 34, 35, 37, 39, 41, 43, 45, 47, 51 and 67 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claims 21, 34, 35, 37, 39, 41, 43, 45, 47, 51 and 67 are vague and indefinite because claims 21 and 67 only describes the polypeptide of interest by an arbitrary name, OB-Re. While the name itself may have some notion of the activity of the protein, there is nothing in the claim which distinctly claims the protein. Others in the field may isolate the same polypeptide and give such an entirely different name. Applicant should particularly point out and distinctly claim the OB-Re protein by claiming characteristics associated with the protein. Claiming biochemical molecules by a particular name given to the protein by various workers in the field fails to claim what the protein is.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

10. Claims 22, 24, 26, 34-48, 51, 52 are rejected under 35 U.S.C. 102(e) as being anticipated by Tartaglia et al., US Patent No. 6,506,877, filing date Dec. 28, 1995.

Claims 22, 24, 26, 34-48, 51, 52 encompass nucleic acids that encode a soluble leptin receptor (OB-R polypeptide) which may be a murine receptor, nucleic acids that hybridize to a DNA molecule of SEQ ID NO: 9, expression vectors, which may be transgenic, host cells that may be E. coli, Saccharomyces, Pichia, CHO cells, and method of preparing polypeptide recombinantly.

Tartalgia et al. disclose human and murine Ob (leptin) receptors (see entire patent), wherein the receptors may be soluble (column 5, lines 32-34, column 8, lines 34-49, column 13, lines 17-19, column 17, lines 54-61, column 31, lines 5-12 for example), and discloses murine Ob (leptin) receptor (SEQ ID NO: 2) that is 100% identical to amino acids 1-796 of SEQ ID NO: 10 of the instant invention, and nucleic acid (SEQ ID NO: 1) which is 98.9% identical to nucleotides 1-2443 of SEQ ID NO: 9 of the instant invention. Those nucleotides are 99.4% of the entire open reading frame (the open reading frame of SEQ ID NO: 9 is nucleotides 44-2457). The nucleic acid of Tartaglia et al. would be hybridizable to a DNA molecule of SEQ ID NO: 9. Tartaglia also teaches expression vectors, which may be transgenic, host cells that may be E.

coli, Saccharomyces, Pichia, CHO cells, and method of preparing polypeptide recombinantly (column 8, lines 3-5, column 13, lines 29-50, column 18, line 5 to column 19, line 62. Therefore Tartaglia et al. et al. anticipates the claims.

Conclusion

11. No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Eileen B. O'Hara, whose telephone number is (703) 308-3312. The examiner can normally be reached on Monday through Friday from 10:00 AM to 6:30 PM. ***Applicant is advised that effective January 23, 2003, the Examiner's phone number will be (571) 272-0878.***

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler can be reached at (703) 308-6564. ***Applicant is advised that effective January 23, 2003, Yvonne Eyler's phone number will be (571) 272-0871.***

Official papers Before Final filed by RightFax should be directed to (703) 872-9306.

Official papers After Final filed by RightFax should be directed to (703) 872-9307.

Official papers filed by fax should be directed to (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Eileen B. O'Hara, Ph.D.

Eileen B. O'Hara

Patent Examiner